L Number	Hits	Search Text	DB	Time stamp
1	8	adenoviral and sequestrin	USPAT; US-PGPUB; EPO; DERWENT	2004/03/23 10:30
2	5	adenoviral and sequestrin and cpg	USPAT; US-PGPUB; EPO; DERWENT	2004/03/23 10:32
3	20	(kreig.inv. or carson.inv.) and cpg	USPAT; US-PGPUB; EPO; DERWENT	2004/03/23 10:32
4	0	(kreig.inv. or carson.inv.) and cpg and sequestrin	USPAT; US-PGPUB; EPO; DERWENT	2004/03/23 10:33
5	4	(kreig.inv. or carson.inv.) and cpg and adenoviral	USPAT; US-PGPUB; EPO; DERWENT	2004/03/23 10:33
6	4	(kreig.inv. or carson.inv.) and cpg and adenoviral and skin	USPAT; US-PGPUB; EPO; DERWENT	2004/03/23 10:35
7	0	(kreig.inv.) and cpg and adenoviral and skin	USPAT; US-PGPUB; EPO; DERWENT	2004/03/23 10:35
8	0	(kreig.inv.) and cpg and adenoviral	USPAT; US-PGPUB; EPO; DERWENT	2004/03/23 10:35
9	0	(kreig.inv.) and cpg and skin	USPAT; US-PGPUB; EPO; DERWENT	2004/03/23 10:35
10	0	(kreig.inv.) and cpg	USPAT; US-PGPUB; EPO; DERWENT	2004/03/23 10:36
11	0	(kreig.inv.) and iss	USPAT; US-PGPUB; EPO; DERWENT	2004/03/23 10:36
12	27	(kreig.inv.)	USPAT; US-PGPUB; EPO; DERWENT	2004/03/23 10:36
13	1075	(krieg.inv.)	USPAT; US-PGPUB; EPO; DERWENT	2004/03/23 10:36
14	56	(krieg.inv.) and cpg	USPAT; US-PGPUB; EPO; DERWENT	2004/03/23 10:37
15	19	(krieg.inv.) and cpg and skin	USPAT; US-PGPUB; EPO; DERWENT	2004/03/23 10:37
16	1	(krieg.inv.) and cpg and skin and adenoviral	USPAT; US-PGPUB; EPO; DERWENT	2004/03/23 10:39
17	0	(krieg.inv.) and cpg and skin and adenoviral and sequestrin	USPAT; US-PGPUB; EPO; DERWENT	2004/03/23 10:41

18	0	(krieg.inv.) and sequestrin	USPAT; US-PGPUB; EPO; DERWENT	2004/03/23 10:41

sion of nucleic acid molecules, and as to terms such as "epitope of interest", "therapeutic", "immune response", "immunological response", "protective immune response", "immunological composition", "immunogenic composition", and "vaccine composition", inter alia, reference is made to U.S. Pat. No. 5,990,091 issued Nov. 23, 1999, and WO 98/00166 and WO 99/60164, and the documents cited therein and the documents of record in the prosecution of that patent and those PCT applications; all of which are incorporated herein by reference. Thus, U.S. Pat. No. 5,990,091 and WO 98/00166 and WO 99/60164 and documents cited therein and documents or record in the prosecution of that patent and those PCT applications, and other documents cited herein or otherwise incorporated herein by reference, can be consulted in the practice of this invention; and, all exogenous nucleic acid molecules, promoters, and vectors cited therein can be used in the practice of this invention. In this regard, mention is also made of U.S. Pat. Nos. 6,004,777, 5,997,878, 5,989,561, 5,976,552, 5,972,597, 5,858,368, 5,863,542, 5,833,975, 5,863,542, 5,843,456, 5,766,598, 5,766,597, 5,762,939, 5,756,102, 5,756,101, 5,494,807, 6,042,838, 6,004,802 and WO 99/53940.

In another embodiment of the invention, the animal is advantageously a vertebrate such as a mammal, bird, reptile, amphibian or fish; more advantageously a human, or a companion or domesticated or food-producing or feed-producing or livestock or game or racing or sport animal such as a cow, a dog, a cat, a goat, a sheep or a pig or a horse, or even fowl such as turkey, ducks or chicken. In an especially advantageous another embodiment of the invention, the vertebrate is a human. In another embodiment of the invention, the genetic vector is a viral vector, a bacterial vector, a protozoan vector, a retrotransposon, a transposon, a virus shell, or a DNA vector. In another embodiment of the invention, the viral vector, the bacterial vector, the protozoan vector and the DNA vector are recombinant vectors. In another embodiment of the invention, the immune response is against influenza A. In another embodiment of the invention, the immune response against influenza A is induced by the genetic vector expressing a gene encoding an influenza hemagglutinin, an influenza nuclear protein, an influenza M2 or a fragment thereof in the animal's cells. In another embodiment of the invention, the genetic vector is selected from the group consisting of viral vector and plasmid DNA. In another embodiment of the invention, the genetic vector is an adenovirus. In another embodiment of the invention, the adenovirus vector is defective in its E1 region. In another embodiment of the invention, the adenovirus vector is defective in its E3 region. In another embodiment of the invention, the adenovirus vector is defective in its E1 anld E3 regions. In another embodiment of the invention, the DNA is in plasmid form. In another embodiment of the invention, the contacting step further comprises disposing the genetic vector containing the gene of interest on a delivery device and applying the device having the genetic vector containing the gene of interest therein to the skin of the animal. In another embodiment of the invention, the genetic vector encodes an immunomodulatory gene, a co-stimulatory gene or a cytokine gene. In another embodiment of the invention, the vector has all viral genes deleted. In another embodiment of the invention, the genetic vector induces an anti-tumor effect in the animal. In a further embodiment of the invention, the genetic vector expresses an oncogene, a tumor-suppressor gene, or a tumor-associated gene.

The present invention also provides a method of non-invasive genetic immunization in an animal, comprising the step of: contacting skin of the animal with a genetic vector in an amount effective to induce immune response in the animal.

Representative examples of antigens which can be used to produce an immune response using the methods of the present invention include influenza hemagglutinin, influenza nuclear protein, influenza M2, tetanus toxin C-fragment, anthrax protective antigen, anthrax lethal factor, rabies glycoprotein, HBV surface antigen, HIV gp 120, HIV gp 160, human carcinoembryonic antigen, malaria CSP, malaria SSP, malaria MSP, malaria pfg, and mycobacterium tuberculosis HSP, etc. Most preferably, the immune response produces a protective effect against neoplasms or infectious pathogens.

The practice of the present invention includes delivering genetic vectors operatively coding for a polypeptide into the outer layer of skin of a vertebrate by a non-invasive procedure for immunizing the animal or for administering a therapeutic. These genetic vectors can be administered to the vertebrate by direct transfer of the genetic material to the skin without utilizing any devices, or by contacting naked skin utilizing a bandage or a bandage-like device. In preferred applications, the genetic vector is in aqueous solution. Vectors reconstituted from lyophilized powder are also acceptable. The vector may encode a complete gene, a fragment of a gene or several genes, gene fragments fused with immune modulatory sequences such as ubiquitin or CpG-rich synthetic DNA, together with transcription/translation signals necessary for expression.

In another embodiment of the present invention, the vector further contains a gene selected from the group consisting of co-stimulatory genes and cytokine genes. In this method the gene is selected from the group consisting of a GM-CSF gene, a B7-1 gene, a B7-2 gene, an interleukin-2 gene, an interleukin-12 gene and interferon genes.

In a further embodiment of the present invention, the response is against *Clostridium tetanus* infection or the vector comprises AdCMV-tetC:IM or pCMV-tetC. In still another embodiment of the method, the exogenous nucleic acid molecule encodes tetanus toxin C-fragment, or an antigen or epitope of tetanus toxin.

The present invention also provides for a method of non-invasively inducing an immune response to influenza A virus comprising the step of. contacting skin of a subject in need of such treatment topically by applying to the skin an immunologically effective amount of a genetic vector encoding for influenza-specific antigens or fragments thereof which induce an anti-influenza effect in the animal following administration. In one embodiment of the method, the genetic vector is selected from the group consisting of viral vector and plasmid DNA. In another embodiment of the method, the genetic vector is an adenovirus. In another embodiment of the method, the adenovirus vector is defective in its E1 and E3 regions. In a further embodiment of the method, the DNA is in plasmid form. In still another embodiment of the method, the contacting step further comprises disposing the genetic vector containing the gene of interest on a delivery device and applying the device having the genetic vector containing the gene of interest therein to the skin of the animal.

Embodiments of the invention that employ adenovirus recombinants, may include E1-defective, E3-defective, and/or E4-defective adenovirus vectors, or the "gutless" adenovirus vector in which all viral genes are deleted. The E1 mutation raises the safety margin of the vector because E1-defective adenovirus mutants are replication incompe-